REMARKS/ARGUMENTS

1. Remarks on the amendment

Claims 1 and 7 have been amended to more specifically define Applicant's claimed invention.

Applicants respectfully submit no new matter has been introduced by the amendments.

2. Response to the Rejections of Claims 1-5, 7 and 9-10 Based Upon 35 USC §103(a)

Claims 1-5, 7 and 9-10 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Komer (U.S. 5,773,422), in view of Miller (U.S. 5,728,719) and McDaniel (U.S. 5,952,372). This rejection is respectfully traversed.

In the Office Action dated April 20, 2007, this rejection is made under 35 U.S.C. §102(b) in error. Furthermore, the references stated in the rejection only include Komer and Miller, however, in the reasoning of the rejection, McDaniel was relied upon also. Applicant's argument submitted herein is based on the assumption that this rejection is made under 35 U.S.C. §103(a) based on Komer (U.S. 5,773,422), in view of Miller (U.S. 5,728,719) and McDaniel (U.S. 5,952,372).

A determination under 35 U.S.C. §103 is whether the claimed invention as a whole would have been obvious to a person of ordinary skill in the art at the time the invention was made. *In re Mayne*, 104 F.3d 1339, 1341, 41 USPQ 2d 1451, 1453 (Fed. Cir. 1997). An obviousness determination is based on underlying factual inquiries including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and prior art; and (4) the objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966), see also *Robotic*

Vision Sys., Inc. v. View Eng'g Inc., 189 F.3d 1370 1376, 51 USPQ 2d 1948, 1953 (Fed. Cir. 1999).

Applicant submits that nothing in the art of record teaches or suggests the subject matter positively recited in independent Claims 1 and 7. As recited in independent Claims 1 and 7, Applicant's claimed dermatological composition consisting of an avermectin compound in an amount effective to treat a group of dermatological conditions and a pharmaceutically acceptable carrier, wherein the effective amount is in a concentration range from about 0.05% to about 0.075% (w/v).

The Examiner states that although Komer does not teach a 0.05-0.075% avermectin, the claimed invention is not patentably distinct over prior art of record when Komer is taken in view of MaDaniel and Miller for two reasons. First, McDaniel teaches 1-5% ivermectin containing topical composition. The Examiner believes that McDaniel's teaching of enhanced penetration by using microliposomes implies lowered amount of active agent is required for equivalent results. Second, Miller teaches a topical composition containing a primary active agent of 5.8% together with 0.005-0.5% avermectin compound. Hence, the skills and techniques to make a composition with a low concentration of avermectin are known.

The Examiner concludes that one would have been motivated to make a product as effective and lowest concentration as possible, because unwanted side effect can be reduced and the industrial applicability can be maximized.

The Examiner further believe that one would have been motivated to combine these references and make the modification, because they are drawn to same technical field (constituted with same ingredients and share common utilities, and pertinent to the problem which applicant concerns about).

Applicant respectfully disagrees.

First, Applicant respectfully points out that Komer teaches away from Applicant's claimed invention.

Applicant's claimed composition contains a low concentration of an avermectin compound. Applicant has found that the instant composition is anti-inflammatory and controls inflammation of the affected area; and it has

antimicrobial property and controls dermal infection of the affected area (see page 19, last paragraph and recitation below in this response). Applicant has further found that this low concentration of avermectin compound is clinically effective in treating transient acantholytic dermatitis, acne miliaris necrotica, acne varioliformis, perioral dermatitis, acneiform eruptions, acne vulgaris, or seborrheic dermatitis.

Applicant has particularly described that the low concentration of avermectin compound is advantageous because it reduces risks of adverse side effects, and reduces the possibility of triggering body's autoimmune responses (page 22, last paragraph of the Specification).

Moreover, Applicant has further described that for some of the diseases, such as perioral dermatitis, the skin on the eyelids can be affected. To treat eyelids, a high concentration of the medicine should be avoided to prevent irritation of the eyes. It is found that a 0.075% ivermectin lotion does not cause eye irritation when it is used on the face, around the eyes, or directly on the eyelids (page 20, last paragraph of the Specification).

On the contrary, Komer teaches a pour-on formula containing 0.5% of ivermectin. More importantly, the objective of Komer's invention is to increase avermectin concentration in a composition. Komer specifically teach that formulations including N-methylpyrrolidone, 2-pyrrolidone or their mixtures have the advantages of providing higher concentration of avermectin (Column 2, lines 47-50 of the reference).

Therefore, Komer teaches the opposite of Applicant's claimed invention.

Second, the deficiencies of Komer are not overcome by McDaniel and Miller, either alone or in combination.

Miller also teaches away from Applicant's claimed invention. More specifically, Miller teaches a composition comprising pyriproxifen or a combination of pyriproxifen and avermectin compound for protecting animals from parasites. Miller teaches that pyriproxifen is the primary active component, and avermectin is used together with the primary active component.

Therefore, Miller fails to teach an avermectin composition in the absence of

other primary active component. In other words, based on Miller's express teaching, Miller's composition is not functional without the primary component pyriproxifen.

This teaching is opposite of Applicant's invention that uses only avermectin as the active component at a low concentration.

Third, McDaniel fail to teach or imply Applicant's claimed invention. More specifically, McDaniel teaches a method of treating a form of rosacea associated with the ectoparasite Demodex by orally administering or topically applying ivermectin to eliminate Demodex Follicuorum mites from hair follicles in affected skin. McDaniel's topical formulation contains 1 to 5% of ivermectin, and the low end of the concentration is more than 10 times higher than the concentration of Applicant's claimed composition.

McDaniel recognizes that for his purpose of eliminating Demodex Follicuorum mites the topical treatment is inferior to the oral administration of ivermectin. McDaniel anticipates the topical treatment would require as long as four weeks to achieve sufficient follicle penetration and effective miticidal activity, and further believes the effect could be enhanced by encapsulating the active agent in microliposomes. However, McDaniel does not teach to reduce the concentration of ivermectin while maintaining the required miticidal activity.

Fourth, from the above analysis, it is apparent that contrary to the Examiner's statement, none of the references shares common utilities with the instant composition, and the prior art's solutions for parasite treatment are not pertinent to the problem which Applicant concerns about. The solution of higher concentrations of avermectin or the use of other more potent chemicals is the opposite of using avermectin compound alone at a low concentration which Applicant has arrived at.

It is important to understand that it is the present Invention who has discovered, for the first time, that the avermectin compound is anti-inflammatory, and this property is sufficient at a low concentration for effective treatment of the dermatological conditions described. The therapeutic effects achieved using a low concentration of avermectin compound, as demonstrated in Examples 4 to 14 of the instant application, is unexpected.

Applicant respectfully requests the Examiner's attention to the most recent decision in *KSR Int'l Co. vs. Teleflex Inc.* In the decision, the Supreme Court stated that it is "important to identify a reason that would have prompted a person of ordinary skill in the art in the relevant field to combine the prior art elements" in the manner claimed.

This is apparent based on the above analysis, the prior art fails to recognize the need and benefit of using low concentration of avermectin compound.

Relied on the opposite teachings of the prior art of record, one ordinary skilled in the art would not be motivated to try to obtain a composition containing a low concentration of avermectin (against Korner or McDaniel's teachings) and in the absence of other primary active component (against Miller's teaching). Moreover, based on the prior art's express teachings, if one combines these references, one would not arrive at Applicant's claimed composition.

In the further aspect, the Examiner alleges that Applicant has not described the "basic and novel properties of the invention" and misconstrues the pharmaceutically acceptable carrier as part of the active component of the claimed composition.

Applicant respectfully points out that the Examiner's statement is far from the facts. For the convenience of discussion, Applicant recites the pertinent description of the instant Specification below:

> "It has been found in an informal clinical trial using the method of the present invention that topical application of ivermectin to skin affected by transient acantholytic dermatitis, acne miliaris necrotica, acne varioliformis, perioral dermatitis, or acneiform eruptions has the following advantageous properties: (1) it removes itching and skin irritation caused by these dermatological conditions; (2) it clears up lesions; (3) it is anti-inflammatory and controls inflammation of the

affected area; (4) it has antimicrobial property and controls dermal infection of the affected area; and (5) it is safe and has no side effects observed in any body locations. (see the paragraph bridging pages 19 and 20 of the Specification as filed).

As such, Applicant has clearly identified that it is the anti-inflammatory property of the avermectin compound, as well as its antimicrobial property, that provide the therapeutic effects in treating these dermatological conditions.

Furthermore, Applicant has also clearly described the property of the carrier of the instant composition:

"The avermectin compound is preferably mixed with a pharmaceutically acceptable carrier or a base which is suitable for topical application to dermal tissues, to form a dermatological composition. Suitable examples of carrier or base include, but not limited to, water, glycols, alcohols, lotions, creams, gels, emulsions, and sprays". (see page 18, second paragraph of the Specification)

Therefore, it is clearly that the carrier or base is merely a vehicle for the active components, and does not possess the anti-inflammatory and antimicrobial properties of the active component.

To further clarify the matter, Applicant has copied below the property of the Cetaphil® moisturizing lotion as stated by the manufacturer on the bottle of the product:

"Cetaphil® moisturizing lotion was formulated specifically for chronic dry, sensitive skin. Contains a superior system of extra-strength emollients and humectants, clinically proven to bind water to the skin and prevent moisture loss.

- Provides long-lasting relief to even severe dry skin.

- Free of lanolins, parabens and fragrances that can irritate sensitive skin. Non-comedogenic."

It is noted that the present inventor is a dermatologist, who has chosen to use Cetaphil® moisturizing lotion because it is free of lanolins, parabens and fragrances that can irritate sensitive skin, and it is non-comedogenic (do not block pores).

Therefore, Applicant has described the "basic and novel properties" of the claimed composition in the Specification as filed.

As discussed above, all three references cited are directed to compositions for parasite treatment, which naturally resulted in high concentrations of avermectin compound or using avermectin compound as an adjuvant of other more potent component. As such, Applicant's claimed composition as defined in Claims 1 and 7 is patentably distinct over the prior art of record.

Accordingly, Applicant maintains that the claimed invention is unobvious in view of the prior art of record.

With regard to Claims 2-5 and 9-10, these claims are dependent upon independent Claims 1 and 7. Under the principles of 35 U.S.C. §112, 4th paragraph, all of the limitations of each independent claim are recited in its respective dependent claims. As described above, independent Claims 1 and 7 is not obvious, as such Claims 2-5 and 9-10 are submitted as being allowable over the art of record.

Accordingly, Applicant respectfully requests withdrawal of the rejection of Claims 1-5, 7 and 9-10 under 35 U.S.C. §103(a).

It is respectfully submitted that Claims 1-5, 7 and 9-10, the pending claims, are now in condition for allowance and such action is respectfully requested.

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Reply to Office Action of April 20, 2007

Applicant's Agent respectfully requests direct telephone communication from the Examiner with a view toward any further action deemed necessary to place the application in final condition for allowance.

8/16/2007
Date of Signature

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